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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TONGUE, LAKIA J	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,536	KODAMA ET AL.	
	Examiner	Art Unit	
	LAKIA J. TONGUE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on June 13, 2008 is acknowledged. Claims 2-5 have been canceled. Claims 6 and 7 have been amended. Claims 6 and 7 are pending and under examination.

Objections/Rejections Withdrawn

1. In view of Applicant's cancellation 4, the rejection of claims 2 and 4 under 35 U.S.C. 103(a) as being unpatentable over Lillehoj et al. (Avian Diseases, 2000; 44; 379-389) further in view of Wells et al. (Antonie van Leeuwenhock, 1996; 70: 317-339) is withdrawn. Cancellation of claims 2 and 4 renders the rejection of said claims moot.

2. In view of Applicant's cancellation of claim 2, the objection of said claim is withdrawn.

3. In view of Applicant's cancellation and amendment, the rejection of claims 2-7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn. Applicant's cancellation of claims 2-5 renders the rejection of said claims moot.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection claims 6 and 7 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for the reasons set forth in the previous Office action. The cancellation of claims 2-5 renders the rejection of said claims moot.

Applicant argues that:

1) The "F3" fraction is shown in Example 1 and is well-known in the art.

2) The recited method includes a defined protein fraction, i.e. F3, to create the antibodies.

Applicant's arguments have been considered, but have not been deemed persuasive.

The claims are drawn to a method for treating chicken coccidiosis, which comprises orally administering to a bird antibodies obtained from an egg of a chicken immunized with the F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria acervulina*.

With regard to Points 1 and 2, the claims as amended recite in part, the F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria acervulina*. It is unclear which F3 antibodies will be effective for treating chicken coccidiosis.

Greenspan et al. (Nature Biotechnology 17: 936-937, 1999) recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes to which the members of the claimed genus of antibodies must

bind, which are critical or essential to the binding, one skilled in the art would not recognize that Applicant had possession of the claimed invention at the time the application was filed.

As previously argued, it is unclear how a single protein (i.e. F3) can be a fraction of proteins from 18 to 27 kD. The letter "s (proteins)" coupled with the range of 18 to 27 kD implies that there is more than one protein or fraction of soluble outer membrane proteins to choose from and that the F3 protein is not the only protein being claimed and/or described.

Moreover, Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Although Applicant has amended the claims, they are not drawn to a specific antibody (i.e. defined) with the claimed specificity. Moreover, the specification does not fully characterize the antigen used to immunize (i.e. a soluble outer membrane protein of 18 to 27 kD from the merozoite of *Eimeria acervulina* outer membrane protein).

The courts have recently decided in Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin (CAFC, 02-1187, 1/20/2004) that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public

depository, the applicant can then claim an antibody by its binding affinity to that described antigen. Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

Moreover, defining epitopes is not an easy task, as evidenced by Greenspan et al. (Nature Biotechnology 17: 936-937, 1999). Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody necessary to define an "epitope" (page 937, column 2).

According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes to which the members of the claimed genus of antibodies must bind, which are critical or essential to the binding, one skilled in the art would not recognize that Applicant had possession of the claimed invention at the time the application was filed.

As previously presented, claims 6 and 7 are drawn to a vast genus of antigenic outer membrane proteins and immunogenic fragments thereof. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or

alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

Moreover, the skilled artisan cannot envision the detailed structure of the encompassed proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written

description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

An adequate written description of the claimed antigenic outer membrane protein or an immunogenic fragment thereof, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).

However, the specification has not provided an adequate showing of which antibodies bind to antigens based solely on their common immunogenicity from among different species. The specification does not provide a written description of the invention of claims 2-7. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of antigenic outer membrane protein or an immunogenic fragment thereof, the skilled artisan could not immediately recognize or distinguish members of the claimed genus having preventive and/or reduced cellular and humoral immunogenicity. Therefore, because the art is

unpredictable, in accordance with the Guidelines, the description of antigenic outer membrane protein or an immunogenic fragment thereof is not deemed representative of the genus of immunogenic compositions to which the claims refer and hence do not meet the written description requirements.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 6 is rejected under 35 U.S.C. 103(a) as being obvious over, Miller et al. (WO 95/03813) and Murray et al. (U.S. Patent 4,727,145).

The claims are drawn to a method for treating chicken coccidiosis, which comprises orally administering to a bird antibodies obtained from an egg of a chicken immunized with the F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria acervulina*.

Miller et al. disclose the use of antibodies in vaccine compositions to provide protection against *Eimeria* infection (see abstract). Miller et al. disclose that the antigens can be derived from any of the known *Eimeria* species including *E. acervulina* (see page 6, lines 1-4).

Miller et al. do not specifically disclose antibodies raised against the F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria*

acervulina.

Murray et al. disclose the use of *Eimeria acervulina* proteins from about 27, 26.5, 26, 24, 23, 22.5, 21.5 and 20 kD that are capable of inducing an immune response in chickens (see column 3, lines 19-25). Moreover, Murray et al. disclose that the immunization is by the oral route (see column 3, lines 30).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use a F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria acervulina* in the methods of Miller et al. because there is a common immunoegencity shared among sporozoite and merozoite of *Eimeria acervulina*. Moreover, since all the claimed elements were known in the prior art one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (see the recent Board decision *Ex parte Smith,* --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d at 1396)*.

One would have had a reasonable expectation, barring evidence to the contrary, that the composition and method would be effective for the prevention or treatment of chicken coccidiosis because Miller et al. disclose that any Eimeria antigen (antibody) can be used.

6. Claim 7 is rejected under 35 U.S.C. 103(a) as being obvious over, Miller et al. (WO 95/03813), Murray et al. (U.S. Patent 4,727,145) and Wells et al. (Antonie van Leeuwenhock, 1996; 70: 317-339).

The claims are drawn to a method for treating chicken coccidiosis, which comprises orally administering to a bird antibodies obtained from an egg of a chicken immunized with the F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria acervulina*, wherein the antibodies are orally administered in combination with a lactic acid bacterium and/or an antibody obtained from an egg of a chicken immunized with *Clostridium perfringens*.

Miller et al. disclose the use of antibodies in vaccine compositions to provide protection against *Eimeria* infection (see abstract). Miller et al. disclose that the antigens can be derived from any of the known *Eimeria* species including *E. acervulina* (see page 6, lines 1-4).

Miller et al. do not specifically disclose antibodies raised against the F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria acervulina* nor do they disclose that the antibodies are orally administered in combination with a lactic acid bacterium.

Murray et al. disclose the use of *Eimeria acervulina* proteins from about 27, 26.5, 26, 24, 23, 22.5, 21.5 and 20 kD that are capable of inducing an immune response in chickens (see column 3, lines 19-25). Moreover, Murray et al. disclose that the immunization is by the oral route (see column 3, lines 30).

Wells et al. disclose the use of lactic acid bacteria as vaccine delivery vehicles. Moreover, Wells et al. disclose that the efficacy of bacterial vectors as vaccines is believed to depend on their invasiveness, capacity to survive and multiple, and on the occurrence of adequate levels of antigen gene expressions *in vivo* (see page 318).

It would have been obvious for one of ordinary skill in the art at the time of the invention to use a F3 fraction of soluble outer membrane proteins of 18 to 27 kD from the merozoite of *Eimeria acervulina* in the methods of Miller et al. because there is a common immunoegencity shared among sporozoite and merozoite of *Eimeria acervulina*. Moreover, since all the claimed elements were known in the prior art one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (see the recent Board decision *Ex parte Smith,* --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d at 1396).*

One would have had a reasonable expectation, barring evidence to the contrary, that the composition and method would be effective for the prevention or treatment of chicken coccidiosis because Miller et al. disclose that any Eimeria antigen (antibody) can be used.

Further, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Miller et al. by combining a lactic acid bacteria to the claimed composition to simplify vaccine distribution and vaccine administration as

well as provide a safe, effective vaccine that is capable of eliciting active immunity (see page 317-introduction).

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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LJT
10/1/08

/Robert A. Zeman/
for Lakia J. Tongue, Examiner of Art Unit 1645
October 14, 2008